Arguments/Remarks

In an effort to focus and advance prosecution, the applicants have canceled claims to methods other than treatment of persistent allergic rhinitis. New claims 22-29 have been added, directed to alternative dosages and methods of administration. Support for these claims can be found, for example, in the paragraph bridging pages 2 and 3 and the remainder of page 3 as well as page 4.

Rejection of claims 10-21 under 35 U.S.C. § 112, first paragraph

The claims were rejected for lacking enablement of methods of inhibition of the various conditions. This rejection has been rendered moot by the amendments presented herein.

Rejection of claims 10-21 under 35 U.S.C. § 102

Claim 10 was rejected as anticipated by Gensthaler. As noted by the Office Gensthaler teaches treatment of patients with **seasonal** allergic rhinitis, not **persistent** allergic rhinitis.

It was clear, at the time of filing, that **persistent** allergic rhinitis is a separate and distinct disease from both **seasonal** and **perennial** allergic rhinitis:

(i) Patients suffering from **persistent** allergic rhinitis are sensitive to both outdoor allergens (*e.g.*, pollens) and indoor allergens (*e.g.*, dust mites). In contrast, patients suffering from **seasonal** and **perennial** allergic rhinitis are only sensitive to one set of these allergens, respectively. (see, *J. Allergy Clin. Immunol.* v. 108, no. 5, S147 (2001)).

(ii) Patients suffering from **persistent** allergic rhinitis show characteristic symptoms for a period of more than 4 days a week and more than 4 weeks per year (see, Specification, page 2, ll 20 - 23; *J. Allergy Clin. Immunol.* v. 108, no. 5, S147 (2001); and "A Pocket Guide for Physicians and Nurses", each provided in the Information Disclosure Statement, submitted concurrently herewith).

(iii) Patients suffering from **persistent** allergic rhinitis show ***different symptoms*** than patients suffering from seasonal or perennial allergic rhinitis. **Persistent** allergic rhinitis patients experience an ongoing inflammatory reaction, particularly in the nose (see, *e.g.*, "A Pocket Guide for Physicians and Nurses", page 7, bullet points 5 and 6) and a higher prevalence of asthma (see, Bousuet, *et al.* Clin. Exp. Allergy

2005; 35:728-732, for example, page 730, under the heading "Co-morbidities." A copy of the reference is provided with this response) .

These differences in causation, duration, and symptoms require a different treatment than seasonal or perennial allergic rhinitis treatments. It is not clear that a treatment for seasonal or perennial allergic rhinitis would be effective in treatment of persistent allergic rhinitis due to the additional symptoms which require treatment in the latter. In particular, medicaments suitable for treating **persistent** allergic rhinitis must show a ***long-term efficacy as well as anti-inflammatory action***.

There is no overlap between the groups of patients suffering from seasonal or perennial allergic rhinitis and those suffering from **persistent** allergic rhinitis. As can be seen in the preceding documents, patients suffering from **persistent** allergic rhinitis cannot be equated with persons with seasonal or perennial allergic rhinitis. Therefore, the teaching of Gensthaler, which is directed to treatment of seasonal allergic rhinitis, cannot anticipate claim 10.

Nor can Gensthaler's teaching of an intended study of the long-term effects of Levocetrizine on patients with persistent allergic rhinitis anticipate claim 10 because Gensthaler does not provide an enabling disclosure. Gensthaler merely informs of an intent to conduct a study on the use of Levocetrizine for the treatment of patients with persistent allergic rhinitis. No other details of the study are provided, *e.g.*, dosage, administration regime, administration route, etc. Without such information one of ordinary skill in the art would not be enabled to practice the method of claim 10 and could not be certain of success. For example, a dosage that is too low or infrequently administered may not successfully treat the condition. The mere statement of an intended clinical trial does not put the claimed invention in the public's possession and, therefore, cannot anticipate claim 10.

In view of the foregoing, the applicants respectfully request reconsideration and withdrawal of the 102(b) rejection over Gensthaler.

Claims 11-12, 14-15, 17, 18, and 20-21 were rejected as anticipated by Gray (WO 94/06429). The Office alleged in that Gray teaches a method of treating symptoms of seasonal and perennial allergic rhinitis through the administration of Levocetirizine. Without acquiescing to this rejection, but merely in his effort to advance prosecution, these claims have been canceled, thereby rendering this rejection moot.

Claims 11-15 and 17-21 were rejected as anticipated by Leynadier *et al.* The Office alleged that Leynadier *et al.* disclosed a method for treating seasonal allergic rhinitis comprising administering 5 mg of the Levocetirizine. Without acquiescing to this rejection, but merely in his effort to advance prosecution, these claims have been canceled, thereby rendering this rejection moot.

Rejection of claims 10 and 16 under 35 U.S.C. § 103(a)

The Office rejected claims 10 and 16 as obvious over Gensthaler in view of Leynadier *et al.* the Office alleged that Gensthaler taught treatment of persistent allergic rhinitis with Levocetirizine but did not teach a dosage. The Office relied on Leynadier *et al.* for its teaching of dosages of 2.5, 5 and 10 mg/day (or about 0.035, 0.07, and a 0.14 mg/kilogram of body weight) dosages of Levocetirizine for the treatment of seasonal allergic rhinitis. The Office reasoned that Leynadier *et al.* provided the motivation to treat a patient having persistent allergic rhinitis with a dose of 0.0005 to about 2 mg per kilogram of body weight because it taught that Levocetirizine was significantly superior to placebo in reducing the symptom severity in patients with **seasonal** allergic rhinitis. For the following reasons, the applicants respectfully traverse.

First, the distinction between **seasonal** allergic rhinitis and **persistent** allergic rhinitis should be noted, as discussed previously. Leynadier *et al.* is directed solely to the treatment of patients with **seasonal** allergic rhinitis. Leynadier *et al.* neither teaches nor suggests anything regarding using Levocetirizine for the treatment of **persistent** allergic rhinitis, as presently claimed. Moreover, because Leynadier *et al.* relates only to treatment of the **seasonal** allergic rhinitis, it provides no teachings regarding what dosage (or routes of administration) may be effective for treating **persistent** allergic rhinitis. Leynadier *et al.* teaches nothing comparing **seasonal** allergic rhinitis with **persistent** allergic rhinitis. In particular, Leynadier *et al.* provides no teachings from which one of ordinary skill in the art could derive a reasonable expectation that the success observed in treating ***seasonal*** allergic rhinitis with the particular agent, dosages, and routes of administration would reasonably be expected to be observed with ***persistent*** allergic rhinitis. Prior to the present application, the results were not predictable.

Gensthaler fails to compensate for this deficiency. Gensthaler also reports on the results of treating patients with **seasonal** allergic rhinitis and note that clinical trials were planned for treating **persistent** allergic rhinitis with Levocetirizine. Gensthaler includes nothing regarding expected

results, merely stating that the study director "hopes that the study … and their treatment will portray a comprehensive view of allergic patients and their treatment over the course of the year."

Clearly **seasonal** allergic rhinitis and **persistent** allergic rhinitis were considered sufficiently distinct as to warrant separate clinical trials. It is well known that development of a new drug for a new indication is inherently accompanied by a high degree of unpredictability. Therefore, one could not be reasonably assured that the successful treatment of seasonal allergic rhinitis (short term administration) would be effective against persistent allergic rhinitis (long term administration), generally, or with the particular dosage range (or routes of administration of the new claims) presently claimed. Again, the results were not predictable *a priori*.

Furthermore, even in 2005, ***three years after*** filing of the instant application, it was not predictable that any results from treatments for seasonal or perennial allergic rhinitis could be applied to treatment of persistent allergic rhinitis. For example, Mullol *et al.* (Therapeutics and Clinical Risk Management 2005: 1(4) 265 – 271. A copy of the reference is provided with this response) states at page 269, second column (emphasis added),

> *The above studies were performed in a variety of patients with AR classified by the classic system in SAR [seasonal allergic rhinitis] and PAR [perennial allergic rhinitis]. It is difficult to guess how this evidence can be translated into the new indication PER [persistent allergic rhinitis] because* ***PER patients are different from SAR and PAR patients***.

In summary, without some indication that treatments of **seasonal** allergic rhinitis are also effective against **persistent** allergic rhinitis one of ordinary skill in the art could not reasonably expect success in treating **persistent** allergic rhinitis (as presently claimed) based upon the agents and parameters successfully employed to treat **seasonal** allergic rhinitis. Without such a teaching, the present claims cannot be obvious over the cited art. Accordingly, reconsideration and withdrawal of this obviousness rejection is respectfully requested.

If the examiner believes a teleconference will advance prosecution, he is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

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